REMARKS

Reconsideration of this application is respectfully requested. Claims 88 and 102 have been amended. Support for this amendment can be found throughout the specification, for example, on page 3, lines 28-30. This amendment adds no new matter.

Substance of the Interview

Applicant thanks Examiner Schwadron for the courtesy of the interview held on January 13, 2010, in which potential claim amendments to address the pending rejections were discussed. The claims have been amended, as discussed, to recite that the secondary structure of the self protein is essentially preserved. As discussed with the Examiner, Applicant submits that this amendment obviates the pending rejections.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 102, 103, 105, and 111 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner contends that it is unpredictable as to what particular substitutions can be made to any particular molecule and result in a mutant analog molecule with the functional attributes recited in the claims. (Office Action at 3.)

Applicant traverses the rejection. Applicant's pending claims recite that the analog is made by substituting one or more peptide fragments in the self-protein with a corresponding number of immunodominant foreign T-cell epitopes selected from ovalbumin, hen egg lysozyme, tetanus toxoid, or diphtheria toxoid T-cell epitopes and that the ***secondary*** structure of the self protein is essentially preserved

such that said analog induces an autoantibody response as evidenced by antibody binding to the unmodified self-protein. Applicant submits that the skilled artisan could envision a multitude of substitutions could be made to any particular molecule, which would result in a mutant analog molecule with the functional attributes recited in the claims.

Applicant's specification, together with well-known teachings in the art, fulfills the written description requirement of 35 U.S.C. § 112, first paragraph. Applicant's specification describes a method for inducing autoantibodies against a self-protein, providing two working examples of self-proteins, ubiquitin (Examples 1-2 & 5-6) and TNFα. (Examples 3-4 & 7-9) Applicant's specification describes a number of different analogs of ubiquitin and TNFα made by molecular biological means. (*Id.* at 11-13.)

Applicant's claims recite a number of well-characterized T-cell epitopes. In addition, a plethora of self proteins was known at the time the application was filed. Applicant's specification need not describe all self-proteins, since these are well-known in the art. *See Hybritech v. Monoclonal Antibodies*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed Cir. 1986).

Using the claimed well-characterized epitopes, analogs of self-proteins could be predictably constructed such that the secondary structure of the self proteins is essentially preserved. This could be performed using routine techniques in the art at the time the application was filed. Applicant's specification need not describe these well-known techniques. *See Hybritech*, 802 F.2d at 1384, 231 USPQ at 94. The Examiner has presented no reasons to believe that such analogs would not induce autoantibody responses as evidenced by antibody binding to the unmodified self-

proteins. In fact, Applicant's specification supports the opposite conclusion, namely, that such analogs would induce autoantibody responses. (*See* Specification, Examples.)

Accordingly, Applicant's specification provides an adequate description of the claimed invention. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 102, 103, 105, and 111 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite in the recitation of the phrase "tertiary structure of the self protein is essentially preserved" because it is unclear what changes to the tertiary structure would or would not be encompassed. (Office Action at 7.)

Applicant traverses the rejection for the reasons set forth in the Response filed May 15, 2009. Moreover, Applicant has amended the pending claims to remove the recitation "tertiary structure." Accordingly, this rejection is moot.

Rejections under 35 U.S.C. § 103(a)

Claim 102 was rejected under 35 U.S.C. § 103(a) as being obvious over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (U.S. Patent 5,716,596) and Bona (U.S. Patent 5,969,109). The Examiner contends that Russell-Jones et al. teaches that foreign T-cell epitopes derived from diphtheria toxoid were known in the art, and that Russell-Jones et al. teaches that Trat T-cell epitopes are inserted into proteins, wherein the insertion of the peptides increases the antibody response into which the Trat peptide has been inserted. (Office Action at 10.) The Examiner contends that Bona et al. teaches that a T-

cell epitope can be substituted into a particular region of a target molecule wherein the T-cell epitope retains immunogenicity. (*Id.*) The Examiner relies on Dean et al. solely to support that somatostatin is a self-protein because of its recognized role in a variety of diseases. (*Id.*) The Examiner concludes that one of skill in the art would have been motivated to combine these teachings. (*Id.* at 11.)

Applicant traverses this rejection for the reasons set forth in the Response filed May 15, 2009. Moreover, Applicant has amended the pending claims to include the recitation that the ***secondary*** structure of the self protein is essentially preserved such that said analog induces an autoantibody response as evidenced by antibody binding to the unmodified self-protein. The cited references do not teach or suggest all of the limitations of Applicant's claimed invention.

Nowhere do any of the cited references teach or suggest substituting any T-cell epitope into a self-protein such that the secondary structure of the self protein is essentially preserved, as recited in the pending claims. Moreover, none of the cited references teach or suggest substituting any of the T-cell epitopes recited in Applicant's claims into a self-protein. In addition, none of the cited references teach or suggest that a self-protein with a T-cell epitope substituted into it can induce an autoantibody response as evidenced by antibody binding to the unmodified self-protein. Without teaching or suggestion of any of these recitations of Applicant's claims, the cited references cannot make Applicant's claims obvious.

Furthermore, none of the cited references provides any expectation of success since none of the cited references describes actually generating and testing a modified self-protein containing a T-cell epitope substituted into the self-protein. Thus, none of the cited references can provide any expectation that a modified self-protein would induce an autoantibody response to the unmodified self-protein, as recited in Applicant's pending claims. Only Applicant's specification provides this expectation of success. Accordingly, the rejection should be withdrawn for these additional reasons.

To support the rejection, the Examiner relies on the Supreme Court's decision in *KSR*, stating: "if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill." (Office Action at 12.) The Examiner's reliance on this statement from KSR is in error. None of the cited references ever actually made and tested a modified self-protein containing a T-cell epitope substituted into a self-protein. Thus, a person of ordinary skill in the art would not have recognized that the insertion of any T-cell epitope would induce an autoantibody response to the unmodified self-protein, as recited in Applicant's pending claims. It is only Applicant's specification that allows the skilled artisan make such a conclusion.

Furthermore, Applicant's self proteins containing T cell epitopes substituted into them exhibit unexpected properties. Applicant's invention resulted in a profound antibody response against the self protein (Specification at 5-6) and an autoantibody response that is not restricted to the known MHC class

II type of the inserted T-cell epitope (*id.* at 6.). The antibodies were induced much faster as compared to the known conjugation technique. (*Id.* at 9.) Accordingly, for these additional reasons, Applicant's invention is not obvious over the cited references.

The rejection for obviousness over Russell-Jones et al. in view of Dean et al. and Bona et al. should be withdrawn. The cited references do not teach or suggest all of the limitations of the pending claims. Also, the cited references do not provide any expectation of success. Furthermore, Applicant's claimed method has unexpected properties. Accordingly, the pending claims cannot be obviousness over the cited references, and Applicant respectfully requests withdrawal of the rejection.

Claim 111 was rejected under 35 U.S.C. § 103(a) as being obvious over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (U.S. Patent 5,716,596) and Bona (U.S. Patent 5,969,109) as applied to claim 102 *supra*, and further in view of Hellman et al. (WO 93/05810) and Le et al. (U.S. Patent 5,698,195). The Examiner relies on Russell-Jones et al., Dean et al., and Bona et al. as rendering obvious the claimed invention except for the use of TNFα. The Examiner contends that Hellman et al. teaches conjugation of a self-protein to a carrier recognized by T helper cells to elicit antibodies and that Le et al. teaches the use of antibodies against TNFα to treat TNFα-mediated diseases.

Applicant traverses the rejection for the reasons presented *supra* with respect to the rejection over Russell-Jones et al. in view of Dean et al. and Bona et al. In addition, neither Hellman et al. nor Le et al. remedies the deficiencies

noted *supra*. That is, neither Hellman et al. nor Le et al. teaches or suggests substituting any T-cell epitope into a self-protein such that the secondary structure of the self protein is essentially preserved, as recited in the pending claims. Moreover, neither Hellman et al. nor Le et al. teaches or suggests substituting any of the T-cell epitopes recited in Applicant's claims into a self-protein. In addition, neither Hellman et al. nor Le et al. teaches or suggests that a self-protein with a T-cell epitope substituted into it can induce an autoantibody response as evidenced by antibody binding to the unmodified self-protein. Thus, Applicant's claimed invention cannot be obvious over the cited references, and Applicant respectfully requests withdrawal of the rejection.

Claims 103 and 105 were rejected under 35 U.S.C. § 103(a) as being obvious over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (U.S. Patent 5,716,596) and Bona (U.S. Patent 5,969,109) as applied to claim 102 *supra*, and further in view of Vitello et al. (US 2003/0099634). The Examiner relies on Russell-Jones et al., Dean et al., and Bona et al. as rendering obvious the claimed invention except for the use of the ovalbumin epitope recited in claim 105. The Examiner contends that Vitello et al. teaches the claimed epitope.

Applicant traverses the rejection for the reasons presented *supra* with respect to the rejection over Russell-Jones et al. in view of Dean et al. and Bona et al. In addition, Vitello et al. does not remedy the deficiencies noted *supra*. That is, Vitello et al. does not teach or suggest substituting any T-cell epitope into a self-protein such that the secondary structure of the self protein is essentially preserved, as recited in the pending claims. Moreover, Vitello et al. does not

teach or suggest substituting any of the T-cell epitopes recited in Applicant's claims into a self-protein. In addition, Vitello et al. does not teach or suggest that a self-protein with a T-cell epitope substituted into it can induce an autoantibody response as evidenced by antibody binding to the unmodified self-protein. Thus, Applicant's claimed invention cannot be obvious over the cited references, and Applicant respectfully requests withdrawal of the rejection.

Applicant submits that this application is in condition for allowance. If the Examiner believes that issues remain to be addressed before a Notice of Allowance, Applicant respectfully requests that the Examiner contact the undersigned to discuss any outstanding issues.

Respectfully submitted,

Law Office of Salvatore Arrigo

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